Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	4538	Gruber.in.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2004/12/17 14:20
L2	5475	griffin.in.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2004/12/17 14:20
L3	3	l1 and l2 and monoclonal	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2004/12/17 14:57
L4	2292	(APC or (activated adj1 protein adj1 C)) same antibody	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/17 14:58
L5	2292	(APC or (activated adj1 protein adj1 "C")) same antibody	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/17 14:59
L6	73	(serine adj1 proteinase) same antibody	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/17 15:05
L7	168	(PCI or (protein adj1 "C" adj1 inhibitor)) same antibody	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/17 15:04
L8	2	l6 and l7	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/17 15:04
L9	897	(APC or (serine adj1 proteinase)) near10 antibody	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/17 15:06
L10	584	(APC or (serine adj1 proteinase)) near5 antibody	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/17 15:06
L11	16	l7 and l10	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/17 15:14
L12	62	complex near8 (APC or (serine adj1 proteinase) or trypsin or chymotrupsin or urokinase or uPA or tPA or PSA or HGKI) near15 (PCI or antitrypsin)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/17 15:25

L13	1	l12 same (cleaved or uncomplex)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/17 15:20
L14	56	l12 and @py<"2004"	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/17 15:26
L15	9	l12 same antibody	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/17 15:27

```
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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  SEP 01   New pricing for the Save Answers for SciFinder Wizard within
                   STN Express with Discover!
 NEWS  4  OCT 28   KOREAPAT now available on STN
 NEWS  5  NOV 18   Current-awareness alerts, saved answer sets, and current
                   search transcripts to be affected by CERAB, COMPUAB, ELCOM,
                   and SOLIDSTATE reloads
 NEWS  6  NOV 30   PHAR reloaded with additional data
 NEWS  7  DEC 01   LISA now available on STN
 NEWS  8  DEC 09   12 databases to be removed from STN on December 31, 2004
 NEWS  9  DEC 15   MEDLINE update schedule for December 2004

 NEWS EXPRESS  OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
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 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
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FILE 'HOME' ENTERED AT 15:38:16 ON 17 DEC 2004

=> file .meeting
'EVENTLINE' IS NOT A VALID FILE NAME
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available.  If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.
ENTER A FILE NAME OR (IGNORE):ignore
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY     SESSION
FULL ESTIMATED COST                                    0.42        0.42

FILE 'AGRICOLA' ENTERED AT 15:39:09 ON 17 DEC 2004
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FILE 'BIOTECHNO' ENTERED AT 15:39:09 ON 17 DEC 2004
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=> antibody(10A)(PCI or antitrypsin)(5A)(APC, thrombin, trypsin, chymotrypsin,
urokinase, uPA, tPA, PSA)
L1            0 FILE AGRICOLA
L2            0 FILE BIOTECHNO
L3            0 FILE CONFSCI
L4            0 FILE HEALSAFE
L5            0 FILE IMSDRUGCONF
L6            0 FILE LIFESCI
L7            0 FILE MEDICONF
L8            0 FILE PASCAL

TOTAL FOR ALL FILES
L9            0 ANTIBODY(10A)(PCI OR ANTITRYPSIN)(5A)(APC, THROMBIN, TRYPSIN,
                CHYMOTRYPSIN, UROKINASE, UPA, TPA, PSA)

=>  antibody(P)(PCI or antitrypsin)(P)(APC, thrombin, trypsin, chymotrypsin,
urokinase, uPA, tPA, PSA)
L10           0 FILE AGRICOLA
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'ANTIBODY(P)(PCI'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'TITRYPSIN)(P)(APC,'
L11           0 FILE BIOTECHNO
L12           0 FILE CONFSCI
L13           0 FILE HEALSAFE
L14           0 FILE IMSDRUGCONF
L15           0 FILE LIFESCI
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'ANTIBODY(P)(PCI'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'TITRYPSIN)(P)(APC,'
L16           0 FILE MEDICONF
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'ANTIBODY(P)(PCI'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'TITRYPSIN)(P)(APC,'
L17           0 FILE PASCAL
```

TOTAL FOR ALL FILES
L18 0 ANTIBODY(P)(PCI OR ANTITRYPSIN)(P)(APC, THROMBIN, TRYPSIN, CHYMO TRYPSIN, UROKINASE, UPA, TPA, PSA)

=> antibody and (PCI or antitrypsin) and (APC, thrombin, trypsin, chymotrypsin, urokinase, uPA, tPA, PSA)
L19 0 FILE AGRICOLA
L20 0 FILE BIOTECHNO
L21 0 FILE CONFSCI
L22 0 FILE HEALSAFE
L23 0 FILE IMSDRUGCONF
L24 0 FILE LIFESCI
L25 0 FILE MEDICONF
L26 0 FILE PASCAL

TOTAL FOR ALL FILES
L27 0 ANTIBODY AND (PCI OR ANTITRYPSIN) AND (APC, THROMBIN, TRYPSIN, CHYMOTRYPSIN, UROKINASE, UPA, TPA, PSA)

=> antibody and (PCI or antitrypsin or (serine proteinase inhibitor) and ((serine proteinase), APC, thrombin, trypsin, chymotrypsin, urokinase, uPA, tPA, PSA)
MISSING OPERATOR ROTEINASE), APC,
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> antibody and (PCI or antitrypsin or (serine proteinase inhibitor)) and ((serine proteinase), APC, thrombin, trypsin, chymotrypsin, urokinase, uPA, tPA, PSA)
MISSING OPERATOR ROTEINASE), APC,
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> antibody and (PCI or antitrypsin) and ((serine proteinase inhibitor), APC, thrombin, trypsin, chymotrypsin, urokinase, uPA, tPA, PSA)
MISSING OPERATOR NHIBITOR), APC,
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> antibody and (PCI or antitrypsin) and ((serine(2A)proteinase(2A)inhibitor)), APC, thrombin, trypsin, chymotrypsin, urokinase, uPA, tPA, PSA)
MISSING OPERATOR NHIBITOR)), APC,
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> antibody and (PCI or antitrypsin) and serine proteinase inhibitor
L28 1 FILE AGRICOLA
L29 22 FILE BIOTECHNO
L30 0 FILE CONFSCI
L31 0 FILE HEALSAFE
L32 0 FILE IMSDRUGCONF
L33 2 FILE LIFESCI
L34 0 FILE MEDICONF
L35 4 FILE PASCAL

TOTAL FOR ALL FILES
L36 29 ANTIBODY AND (PCI OR ANTITRYPSIN) AND SERINE PROTEINASE INHIBITOR

=> antibody(7A)(PCI or antitrypsin)(7A)(serine proteinase inhibitor)
L37 0 FILE AGRICOLA
L38 0 FILE BIOTECHNO
L39 0 FILE CONFSCI
L40 0 FILE HEALSAFE
L41 0 FILE IMSDRUGCONF
L42 0 FILE LIFESCI

```
L43             0 FILE MEDICONF
L44             0 FILE PASCAL

TOTAL FOR ALL FILES
L45             0 ANTIBODY(7A)(PCI OR ANTITRYPSIN)(7A)(SERINE PROTEINASE INHIBITOR
                  )

=>  antibody(12A)(PCI or antitrypsin)(10A)(serine proteinase inhibitor)
L46             0 FILE AGRICOLA
L47             0 FILE BIOTECHNO
L48             0 FILE CONFSCI
L49             0 FILE HEALSAFE
L50             0 FILE IMSDRUGCONF
L51             0 FILE LIFESCI
L52             0 FILE MEDICONF
L53             0 FILE PASCAL

TOTAL FOR ALL FILES
L54             0 ANTIBODY(12A)(PCI OR ANTITRYPSIN)(10A)(SERINE PROTEINASE INHIBIT
                  OR)

=> antibody and complex and (PCI or antitrypsin) and (APC, thrombin, trypsin,
chymotrypsin, urokinase, uPA, tPA, PSA, (serine proteinase inhibitor))
MISSING OPERATOR 'PSA, (SERINE'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=>  antibody and complex and (PCI or antitrypsin) and (thrombin, trypsin,
chymotrypsin, urokinase, uPA, tPA, PSA, (serine proteinase inhibitor))
MISSING OPERATOR 'PSA, (SERINE'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> dup rem
ENTER L# LIST OR (END):136
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L36
L55            26 DUP REM L36 (3 DUPLICATES REMOVED)

=> l55 and py<2001
L56             1 S L55
L57             1 FILE AGRICOLA
L58            22 S L55
L59            20 FILE BIOTECHNO
L60             0 S L55
'2001' NOT A VALID FIELD CODE
L61             0 FILE CONFSCI
L62             0 S L55
L63             0 FILE HEALSAFE
L64             0 S L55
L65             0 FILE IMSDRUGCONF
L66             1 S L55
L67             0 FILE LIFESCI
L68             0 S L55
'2001' NOT A VALID FIELD CODE
L69             0 FILE MEDICONF
L70             2 S L55
L71             0 FILE PASCAL

TOTAL FOR ALL FILES
L72            21 L55 AND PY<2001

=> d l72 ibib abs total
```

L72 ANSWER 1 OF 21 AGRICOLA Compiled and distributed by the National Agricultural Library of the Department of Agriculture of the United States of America. It contains copyrighted materials. All rights reserved. (2004) on STN

ACCESSION NUMBER: 94:29210 AGRICOLA
DOCUMENT NUMBER: IND20384544
TITLE: Isolation and characterization of native bovine milk plasminogen activators.
AUTHOR(S): Lu, D.D.; Nielsen, S.S.
AVAILABILITY: DNAL (44.8 J822)
SOURCE: Journal of dairy science, **Nov 1993.** Vol. 76, No. 11. p. 3369-3383
Publisher: Champaign, Ill. : American Dairy Science Association.
CODEN: JDSCAE; ISSN: 0022-0302
NOTE: Includes references
PUB. COUNTRY: Illinois; United States
DOCUMENT TYPE: Article
FILE SEGMENT: U.S. Imprints not USDA, Experiment or Extension
LANGUAGE: English

AB Plasminogen activators were partially purified from fresh bovine skim milk by treatments with sulfuric acid, ammonium sulfate, and dimethylformamide, followed by Zn-chelating chromatography, resulting in a purification factor of 2204-fold for skim milk, which contained 340 mU/L of plasminogen activator activity as measured by a colorimetric assay. Further purification with plasminogen activator inhibitor affinity chromatography gave purification factors of about 11,000-fold, but plasminogen activators in this fraction were not stable. The plasminogen activators obtained from Zn-chelating chromatography were characterized for molecular mass, urokinase-type versus tissue-type, and susceptibility to protease inhibitors. Five bands with plasminogen activator activity were detected by casein-plasminogen SDS-PAGE with molecular mass of approximately 93, 57, 42, 35, and 27 kDa. Most or all of the plasminogen activators in bovine milk were urokinase-type; the activity of the bovine milk plasminogen activators was not enhanced by the presence of fibrin. The immunological dissimilarity between bovine milk plasminogen activators and human urokinase-type plasminogen activator and human tissue-type plasminogen activator was shown by **antibody** quenching tests. Bovine milk plasminogen activators were inhibited by certain **serine proteinase inhibitors**, endothelial cell-type plasminogen activator inhibitor, plasminogen activator inhibitor from erythrina seed, and alpha 2-antiplasmin, but not by alpha 1-**antitrypsin**.

L72 ANSWER 2 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 1999:29373183 BIOTECHNO
TITLE: Purification and characterization of serum serpin from carp (Cyprinus carpio)
AUTHOR: Aranishi F.
CORPORATE SOURCE: F. Aranishi, Div. of Physiology/Molecular Biology, Natl. Res. Inst. of Fisheries Sci., Yokohama 236-8648, Japan.
E-mail: aranishi@nrifs.affrc.go.jp
SOURCE: Marine Biotechnology, (**1999**), 1/1 (81-88), 23 reference(s)
CODEN: MABIFW ISSN: 1436-2228
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 1999:29373183 BIOTECHNO

AB A **serine proteinase inhibitor**, termed serpin62, was purified to homogeneity from carp serum with an increase in

specific inhibitory activity of 6.2-fold and a 3% recovery rate after separation from α.sub.1- **antitrypsin**. Specific inhibitory activity of serpin62 against bovine pancreatic trypsin was less than half of the specific antitryptic activity of α.sub.1- **antitrypsin** . Under both reducing and nonreducing conditions, serpin62 was estimated to have a molecular weight (62,000) apparently larger than that of α.sub.1- **antitrypsin** (55,000). They both consist of single polypeptide chains, but serpin62 differs from **serine proteinase inhibitors** from muscles of carp and white croaker in molecular weight and structure. **Antibody** raised against serpin62 immunologically crossreacted with serpin62 and had no crossreactivity with fish serum α.sub.1- **antitrypsin** and muscular analogues. The **antibody** was susceptible to both serpin62 and its derivatives, which were widely distributed in carp tissues. Serpin62 is most likely distinct from other fish **serine proteinase inhibitors** expressing antitryptic activity physicochemically and immunologically.

L72 ANSWER 3 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1999:29366495 BIOTECHNO
TITLE: Strategies for novel COPD therapies
AUTHOR: Barnes P.J.
CORPORATE SOURCE: P.J. Barnes, National Heart and Lung Institute, Imperial College School of Medicine, Dovehouse Street, London SW3 6LY, United Kingdom.
SOURCE: Pulmonary Pharmacology and Therapeutics, (**1999**), 12/2 (67-71), 15 reference(s)
CODEN: PPTHFJ ISSN: 1094-5539
DOCUMENT TYPE: Journal; Conference Article
COUNTRY: United Kingdom
LANGUAGE: English
AN 1999:29366495 BIOTECHNO

L72 ANSWER 4 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1997:27425766 BIOTECHNO
TITLE: Antineutrophil cytoplasmic **antibodies** induce monocyte IL-8 release: Role of surface proteinase-3, α1- **antitrypsin**, and Fcγ receptors
AUTHOR: Ralston D.R.; Marsh C.B.; Lowe M.P.; Wewers M.D.
CORPORATE SOURCE: Dr. M.D. Wewers, Div. of Pulmonary/Critical Care Med., Ohio State University Medical Center, 1654 Upham Drive, Columbus, OH 43210, United States.
E-mail: wewers.2@osu.edu
SOURCE: Journal of Clinical Investigation, (**1997**), 100/6 (1416-1424), 22 reference(s)
CODEN: JCINAO ISSN: 0021-9738
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1997:27425766 BIOTECHNO
AB Cytoplasmic antineutrophii cytoplasmic **antibodies** (cANCA) that accompany the neutrophilic vasculitis seen in Wegener's granulomatosis (WG), are directed against proteinase-3 (PR-3), a serine proteinase which is located in azurophilic granules of neutrophils and monocytes. PR-3, when expressed on the surface of TNFα-primed neutrophils, can directly activate neutrophils by complexing cANCA and promoting concomitant Fcγ receptor (FcγR) cross- linking. Although the neutrophil's pathogenic role in WG has been studied, the role of the monocyte has not been explored. The monocyte, with its ability to release cytokines and regulate neutrophil influx, also expresses PR-3. Therefore, the monocyte may play a significant role in WG via the interaction of surface PR-3 with cANCA, inducing cytokine release by the monocyte. To

test this hypothesis, monocytes were studied for PR-3 expression and for IL-8 release in response to cANCA IgG. PBMC obtained from healthy donors displayed dramatic surface PR-3 expression as detected by immunohistochemistry and flow cytometry in response to 0.5-h pulse with TNFα (2 ng/ml). Purified monoclonal anti-PR-3 IgG added to TNFα-primed PBMC induced 45-fold more IL-8 release than an isotype control **antibody**. Furthermore, alpha 1-**antitrypsin** (α1-AT), the primary PR-3 antiprotease, inhibited the anti-PR-3 induced IL-8 release by 80%. Importantly, Fab and F(ab').sub.2 fragments of anti-PR-3 IgG, which do not result in Fcγ receptor cross-linking, do not induce IL-8 release. As a correlate, IgG isolated from cANCA positive patients with WG induced six times as much PBMC IL-8 release as compared to IgG isolated from normal healthy volunteers. Consistent with PR-3 associated IL-8 induction, α1-AT significantly inhibited this effect. These observations suggest that cANCA may recruit and target neutrophils through promoting monocyte IL-8 release. This induction is mediated via Fcγ receptor cross-linking and is regulated in part by α1-AT.

L72 ANSWER 5 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1997:27360159 BIOTECHNO
TITLE: Gene expression of proteases and protease inhibitors in the human ciliary epithelium and ODM-2 cells
AUTHOR: Ortego J.; Escribano J.; Coca-Prados M.
CORPORATE SOURCE: M. Coca-Prados, Dept. of Ophthalmology/Visual Sci., Yale University School of Medicine, 330 Cedar St., New Haven, CT 06510, United States.
SOURCE: Experimental Eye Research, (**1997**), 65/2 (289-299), 46 reference(s)
CODEN: EXERA6 ISSN: 0014-4835
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1997:27360159 BIOTECHNO
AB Complementary DNAs (cDNAs), corresponding to the human proteinases cathepsins D and O and proteinase inhibitors α2-macroglobulin and PP5/TFPI- 2, have recently been isolated and identified from a subtractive human ciliary body library. In the present study we determined: (i) their pattern of expression in the human eye; (ii) the ability of the ciliary body and/or ciliary epithelial cells to synthesize and secrete cathepsin D and α1- **antitrypsin** in vitro; and (iii) whether α1- **antitrypsin** expression in cultured ciliary epithelial cells is modulated by protein kinase C activation. Northern analysis demonstrated that the ciliary body expresses high levels of cathepsins D and O, α2-macroglobulin, α1- **antitrypsin** and PP5/TFPI-2 transcripts. Western blot analysis and immunoprecipitation experiments with cathepsin D and α1- **antitrypsin antibodies** indicated that metabolically labeled ciliary body explants and/or ciliary epithelial cells in vitro with .sup.3.sup.5S-methionine, synthesize find secrete these proteins. Cultured nonpigmented ciliary epithelial ODM-2 cells, in response to phorbol- 12-myristate 13-acetate (PMA), but not to the non-protein kinase C binding phorbol ester 4 α-phorbol didecanoate (PDBu), elicited up-regulation (up to 5-fold) of transcription, synthesis and secretion of α1- **antitrypsin**. These results provide in vitro evidence that the ciliary epithelium synthesizes and secretes a selective group of proteinases and proteinase inhibitors detected also in aqueous humor. The expression of at least of one of the proteinase inhibitors, α1- **antitrypsin**, can be modulated in response to phorbol ester.

L72 ANSWER 6 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1997:27357053 BIOTECHNO
TITLE: Serine protease inhibitors in patients with chronic

viral hepatitis
AUTHOR: Elzouki A.-N.; Verbaan H.; Lindgren S.; Widell A.; Carlson J.; Eriksson S.
CORPORATE SOURCE: Prof. S. Eriksson, Department of Medicine, University Hospital, S-205 02 Malmo, Sweden.
SOURCE: Journal of Hepatology, (**1997**), 27/1 (42-48), 33 reference(s)
CODEN: JOHEEC ISSN: 0168-8278
DOCUMENT TYPE: Journal; Article
COUNTRY: Denmark
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1997:27357053 BIOTECHNO
AB Background/Aims: This study aimed to determine whether deficiency of the major serine protease inhibitors (α.sub.1- **antitrypsin** (AAT) or α.sub.1- antichymotrypsin (ACT)) is associated with increased risk for chronic hepatitis B or C virus (HBV or HCV) infection. Methods: We studied 709 adults with chronic liver disease who had undergone liver biopsy during the 14-year period 1978-92. Anti-HCV testing was carried out with second-generation ELISA and immunoblot assays (RIBA 2). HBV markers were tested with commercially available radioimmunoassays. ACT and AAT concentrations in plasma were measured with electroimmunoassay and immune nephelometry. Plasma samples were screened for the AAT PiZ deficiency with ELISA technique and phenotyped by isoelectric focusing. The .sup.2.sup.2.sup.9Pro→Ala mutation for ACT deficiency was identified by PCR techniques. Results: Of the 709 patients, 132 (18.6%) were positive for anti-HCV according to RIBA 2. PiZ AAT deficiency was found in 44 (6.2%) of patients (one PiZZ, 38 PiMZ, and PiSZ), while subnormal ACT levels were found in 33 (4.6%) patients, frequencies that were higher than expected in the general population ($p=0.0375$ and $p<0.0001$, respectively). Of the PiZ- carriers, 8/44 (18%) were found to be anti-HCV positive according to RIBA 2, as compared to 123/662 (19%) non-PiZ-carriers ($p>0.05$). One of these patients had cirrhosis, four chronic active hepatitis, and three chronic persistent hepatitis. In contrast, 17/33 (51.5%) of the patients with subnormal ACT were anti-HCV positive (OR=5.2, CI=2.6-10.6; $p<0.0001$). No relationship was found between HBV infection and AAT deficiency or subnormal ACT levels. Only one patient with subnormal ACT levels was heterozygous for the .sup.2.sup.2.sup.9Pro→Ala mutation of ACT deficiency. There was no significant difference in the histological findings when the patients with subnormal ACT levels or PiZ allele were subgrouped according to HCV status. Conclusions: There is no overrepresentation of chronic HBV or HCV in heterozygous AAT deficiency, although an association with more severe liver disease in such patients cannot be excluded. In contrast, low plasma levels of ACT that may be acquired or hereditary, due to mutations other than .sup.2.sup.2.sup.9Pro→Ala, are frequent in HCV infection.

L72 ANSWER 7 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1997:27170865 BIOTECHNO
TITLE: Linear polymerization caused by the defective folding of a non-inhibitory serpin ovalbumin
AUTHOR: Shirai N.; Tani F.; Higasa T.; Yasumoto K.
CORPORATE SOURCE: F. Tani, Research Institute for Food Science, Kyoto University, Uji, Kyoto 611, Japan.
E-mail: tani@soya.food.kyoto-u.ac.jp
SOURCE: Journal of Biochemistry, (**1997**), 121/4 (787-797), 49 reference(s)
CODEN: JOBIAO ISSN: 0021-924X
DOCUMENT TYPE: Journal; Article
COUNTRY: Japan
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1997:27170865 BIOTECHNO

AB Polymerization caused by defective folding of heat-denatured ovalbumin was examined. A compactly misfolded ovalbumin that was produced by cooling heat-denatured protein rapidly tended to aggregate in the presence of salt. Two different forms of aggregates were observed as the concentration of salt was varied: a linear polymer at a physiological concentration and a massive agglomerate at a higher concentration. Salt-induced polymerization depended on the species of anion and the order of effectiveness followed the lyotropic series of Hofmeister. Defective folding of heat-denatured ovalbumin induced the exposure of cysteine residues in sequences located in the interior of the native protein. The misfolded ovalbumin, but not the native protein, bound to bovine BiP and stimulated its ATPase activity with the K(m) of 64 μM and the V(max) of 0.5 nmol/min per milligram. Measurement of surface plasmon resonance revealed that only the misfolded ovalbumin was recognized with the K(d) of 4.12 x 10.sup.-.sup.8 M by the Fab fragment of a monoclonal **antibody** raised against hen ovalbumin, and its epitope was determined to be a hydrophobic segment in the β-strand of central sheet A. Transmission electron microscopy showed that the linear polymerization was inhibited by the addition of bovine BiP and the Fab fragment. These results demonstrated that the compactly misfolded ovalbumin polymerized through hydrophobic interaction occurring among the areas exposed as a result of defective folding of the heat-denatured protein. Exposure of the region of, or adjacent to, the central β-sheet A was required for axial contact among the misfolded molecules, suggesting that this process may be explained by reference to the mechanism proposed for loop-sheet polymerization in the Z type variant of a serpin α.sub.1- **antitrypsin**.

L72 ANSWER 8 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1996:26139171 BIOTECHNO
TITLE: Structural investigation of the alpha-1-antichymotrypsin: Prostate- specific antigen complex by comparative model building
AUTHOR: Villoutreix B.O.; Lilja H.; Pettersson K.; Lovgren T.; Teleman O.
CORPORATE SOURCE: Technical Research Centre of Finland, VTT Biotechnology and Food Research, POB 1500,FIN-02044 VTT (Espoo), Finland.
SOURCE: Protein Science, (**1996**), 5/5 (836-851)
CODEN: PRCIEI ISSN: 0961-8368
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1996:26139171 BIOTECHNO
AB Prostate-specific antigen (PSA), produced by prostate cells, provides an excellent serum marker for prostate cancer. It belongs to the human kallikrein family of enzymes, a second prostate-derived member of which is human glandular kallikrein-1 (hK2). Active PSA and hK2 are both 237-residue kallikrein-like proteases, based on sequence homology. An hK2 model structure based on the serine protease fold is presented and compared to PSA and six other serine proteases in order to analyze in depth the role of the surface- accessible loops surrounding the active site. The results show that PSA and hK2 share extensive structural similarity and that most amino acid replacements are centered on the loops surrounding the active site. Furthermore, the electrostatic potential surfaces are very similar for PSA and hK2. PSA interacts with at least two serine protease inhibitors (serpins): alpha-1-antichymotrypsin (ACT) and protein C inhibitor (**PCI**). Three-dimensional model structures of the uncleaved ACT molecule were developed based upon the recent X-ray structure of uncleaved antithrombin. The serpin was docked both to PSA and hK2. Amino acid replacements and electrostatic complementarities indicate that the overall orientation of the proteins in these complexes is reasonable. In

order to investigate PSA's heparin interaction sites, electrostatic computations were carried out on PSA, hK2, protein C, ACT, and **PCI**. Two heparin binding sites are suggested on the PSA surface and could explain the enhanced complex formation between PSA and **PCI**, while inhibiting the formation of the ACT-PSA complex. PSA, hK2, and their preliminary complexes with ACT should facilitate the understanding and prediction of structural and functional properties for these important proteins also with respect to prostate diseases.

L72 ANSWER 9 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1996:26095468 BIOTECHNO
TITLE: Cellular internalization and degradation of antithrombin III-thrombin, heparin cofactor II-thrombin, and α.sub.1- **antitrypsin** -trypsin complexes is mediated by the low density lipoprotein receptor-related protein
AUTHOR: Kounnas M.Z.; Church F.C.; Argraves W.S.; Strickland D.K.
CORPORATE SOURCE: 15601 Crabbs Branch Way,Rockville, MD 20855, United States.
SOURCE: Journal of Biological Chemistry, (**1996**), 271/11 (6523-6529)
CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1996:26095468 BIOTECHNO
AB The inhibition of proteinase activity by members of the **serine proteinase inhibitor** (serpin) family is a critical regulatory mechanism for a variety of biological processes. Once formed, the serpin enzyme complexes (SECs) are removed from the circulation by a hepatic receptor. The present study suggests that this receptor is very likely the low density lipoprotein receptor-related protein (LRP), a prominent liver receptor. In vitro binding studies revealed that antithrombin III (ATIII) .midldot. thrombin, heparin cofactor II (HCII) .midldot. thrombin, and α.sub.1- **antitrypsin** (α.sub.1AT) .midldot. trypsin bound to purified LRP, and their binding was inhibited by the 39-kDa receptor- associated protein (RAP), an antagonist of LRP-ligand binding activity. In contrast, native or modified forms of the inhibitors were unable to bind to LRP. Mouse embryonic fibroblasts, which express LRP, mediate the cellular internalization leading to degradation of these SECs, while mouse fibroblasts genetically deficient in LRP showed no capacity to internalize and degrade these complexes. SECs were also degraded by HepG2 cells, and this process was inhibited by LRP **antibodies**, RAP, and chloroquine. The cellular-mediated uptake and degradation was specific for SECs; native or modified forms of the inhibitors were not internalized and degraded. Finally, in vivo clearance studies in rats demonstrated that RAP inhibited the clearance of ATIII .midldot. .sup.1.sup.2.sup.5I-thrombin complexes from the circulation. Together, these results indicate that LRP functions as a liver receptor responsible for the plasma clearance of SECs.

L72 ANSWER 10 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1995:25057248 BIOTECHNO
TITLE: Differential recognition of α.sub.1-**antitrypsin**-elastase and α.sub.1-antichymotrypsin-cathepsin G complexes by the low density lipoprotein receptor-related protein
AUTHOR: Poller W.; Willnow T.E.; Hilpert J.; Herz J.
CORPORATE SOURCE: Medical University Clinic, Clinical Biochem./Pathobiochemistry, Versbacher Strasse 5,D-97080 Wurzburg, Germany.

SOURCE: Journal of Biological Chemistry, (**1995**), 270/6 (2841-2845)
CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1995:25057248 BIOTECHNO
AB Two multifunctional receptors, low density lipoprotein receptor-related protein (LRP) and gp330, have been implicated in the cellular uptake and degradation of a wide spectrum of functionally diverse ligands including plasma lipoproteins, proteases, and proteinase-inhibitor complexes. The two receptors show distinct tissue-specific expression patterns, suggesting different physiological functions. We have examined the cellular degradation of two **serine proteinase inhibitor** (serpin)-protease complexes, α.sub.1-**antitrypsin**-neutrophil elastase (α.sub.1AT.midldot.NEL) and α.sub.1-antichymotrypsin- cathepsin G (α.sub.1ACT.midldot.Cat hG) by normal murine fibroblasts (MEF) expressing LRP, and by a mutant flbroblast çell line (PEA13) which is genetically deficient for LRP. α.sub.1AT.midldot.NEL complexes bound to LRP on ligand blots and were degraded efficiently by the MEF cells, but not by PEA13 cells. Degradation of the complexes was also significantly reduced by **antibodies** directed against LRP, further suggesting that fibroblasts require LRP for the cellular uptake and degradation of α.sub.1AT.midldot.NEL complexes. In contrast to α.sub.1AT.midldot.NEL, MEF cells did not degrade α.sub.1ACT.midldot.CathG complexes. However, these complexes were rapidly degraded by the rat embryonal carcinoma cell line L2p58 which abundantly expresses gp330, raising the possibility that the α.sub.1ACT.midldot.CathG complex might be recognized by gp330. Both complexes were efficiently metabolized by the hepatoma cell line HepG2, presumably involving the serpin-enzyme complex receptor. The differential recognition of serpin- protease complexes by fibroblasts and hepatoma cells, however, indicates that LRP, gp330, and the serpin-enzyme complex receptor are distinct proteins.

L72 ANSWER 11 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1995:25057209 BIOTECHNO
TITLE: COOH-terminal substitutions in the serpin C1 inhibitor that cause loop overinsertion and subsequent multimerization
AUTHOR: Eldering E.; Verpy E.; Roem D.; Meo T.; Tosi M.
CORPORATE SOURCE: Dept. of Autoimmune-diseases, CLRCBTS, Plesmanlaan 125,1066 CX Amsterdam, Netherlands.
SOURCE: Journal of Biological Chemistry, (**1995**), 270/6 (2579-2587)
CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1995:25057209 BIOTECHNO
AB The region COOH-terminal to the reactive center loop is highly conserved in the serine protease inhibitor (serpin) family. We have studied the structural consequences of three substitutions (Val.sup.4.sup.5.sup.1 → Met, Phe.sup.4.sup.5.sup.5 → Ser, and Pro.sup.4.sup.7.sup.6 → Ser) found in this region of C1 inhibitor in patients suffering from hereditary angioedema. Equivalent substitutions have been described in α1- **antitrypsin** and antithrombin III. The mutant C1 inhibitor proteins were only partially secreted upon transient transfection into COS-7 cells and were found to be dysfunctional. Immunoprecipitation of conditioned media demonstrated that in the intact, uncleaved form they all bind to a monoclonal

antibody which recognizes specifically the protease- complexed or reactive center-cleaved normal C1 inhibitor. A second indication for an intrinsic conformational change was the increased thermostability compared to the normal protein. Furthermore, gel filtration studies showed that the Val.sup.4.sup.5.sup.1 → Met and Pro.sup.4.sup.7.sup.6 → Ser mutant proteins, and to a lesser extent Phe.sup.4.sup.5.sup.5 → Ser, were prone to spontaneous multimerization. Finally, a reduced susceptibility to reactive center cleavage by trypsin was observed for all three mutants, and the cleaved Val.sup.4.sup.5.sup.1 → Met and Pro.sup.4.sup.7.sup.6 → Ser mutants failed to adopt the conformation recognized by a cleavage-specific monoclonal **antibody**. Investigation of plasmas of patients with the Val.sup.4.sup.5.sup.1 → Met or Pro.sup.4.sup.7.sup.6 → Ser substitutions showed that these dysfunctional proteins circulate at low levels and are recognized by the complex-specific **antibody**. These results strongly indicate a conformational change as a result of these carboxyl-terminal substitutions, such that anchoring of the reactive center loop at the COOH-terminal side is not achieved properly. We propose that this results in over-insertion of the loop into β-sheet A, which subsequently leads to multimerization.

L72 ANSWER 12 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1994:24317315 BIOTECHNO
TITLE: Characterization of two serpins from bovine plasma and milk
AUTHOR: Christensen S.; Sottrup-Jensen L.
CORPORATE SOURCE: Department of Molecular Biology, Bldg 130, University of Aarhus,DK-8000 Arhus C, Denmark.
SOURCE: Biochemical Journal, (**1994**), 303/2 (383-390)
CODEN: BIJOAK ISSN: 0264-6021
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1994:24317315 BIOTECHNO
AB An inhibitor of pancreatic elastase (EI), which can also inhibit chymotrypsin, and an inhibitor of trypsin (TI), which can also inhibit plasmin, have been isolated from bovine plasma. EI and TI belong to the serpin family of inhibitors. The size of both inhibitors is approx. 60 kDa and they are able to form SDS-stable complexes with proteinases. Curiously, TI dimerizes in the presence of SDS, a feature which has been observed previously only in non-denaturing gels of human α.sub.1-**antitrypsin** (α.sub.1PI). EI and TI are glycosylated ¢16% and 19% (w/w) respectively! and their amino acid compositions are similar to those of other plasma serpins. Neither EI nor TI is the equivalent of bovine α.sub.1PI, as revealed by partial sequence analysis of their N-termini and reactive sites. Rather, both inhibitors appear to be related to human α.sub.1-antichymotrypsin. Inhibition of pancreatic elastase and chymotrypsin by EI occurs with a k(ass) .sim. 10.sup.5 M.sup.-.sup.1.s.sup.-.sup.1. TI inhibits trypsin with a k(ass) .sim. 10.sup.5 M.sup.-.sup.1.s.sup.-.sup.1. Plasmin is inhibited by TI with a k(ass) .sim. 10.sup.3 M.sup.-.sup.1.s.sup.-.sup.1. The values of the kinetic constants are similar to those determined for the well-studied human serpins. **Antibodies** to EI and TI reveal a set of four antigenically related proteins of similar size in plasma. In addition, they detect the same set of proteins in milk. The inhibitors isolated from milk are identical to EI and TI from plasma. El could control the activity of chymotrypsin-like proteinases in milk. In contrast, no target proteinases of TI in milk can be suggested.

L72 ANSWER 13 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1994:24116012 BIOTECHNO
TITLE: Murine heparin cofactor II: Purification, cDNA

sequence, expression, and gene structure
AUTHOR: Guang Sen Zhang; Mehringer J.H.; Van Deerlin V.M.D.; Kozak C.A.; Tollefsen D.M.
CORPORATE SOURCE: Division of Hematology-Oncology, Washington Univ. School of Medicine, Box 8125, 660 South Euclid Ave.,St. Louis, MO 63110, United States.
SOURCE: Biochemistry, (**1994**), 33/12 (3632-3642)
CODEN: BICHAW ISSN: 0006-2960
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1994:24116012 BIOTECHNO
AB Heparin cofactor II (HCII) is a glycoprotein in human plasma that inhibits thrombin rapidly in the presence of dermatan sulfate or heparin. Unexpectedly, we found that HCII activity in murine plasma is present in two proteins of 68 and 72 kDa. The two proteins have the same N-terminal amino acid sequence, and both react with an **antibody** raised against the C-terminal nine amino acid residues of murine HCII predicted from the cDNA sequence. Treatment of the two proteins with peptide-N.sup.4-(N-acetyl-β- glucosaminyl)asparagine amidase yields a single 54-kDa band. Thus, murine plasma contains two forms of HCII that appear to have identical amino acid sequences but differ in the composition of their N-linked oligosaccharides. HCII cDNA clones isolated from a murine liver library include a 1434 bp open reading frame following the first Met codon, a TAA stop codon, and 580 bp of 3'-untranslated sequence terminating in a poly(A) tail. The amino acid sequence deduced from the cDNA contains the N-terminal sequence of purified murine plasma HCII preceded by a 23-residue hydrophobic sequence presumed to be the signal peptide. The amino acid sequence of murine HCII is 87% identical to that of human HCII, the greatest variability occurring in the N- terminal portion of the protein. Northern blot analysis reveals a 2.3-kb HCII mRNA in murine and human liver, but no HCII mRNA is detectable in heart, brain, spleen, lung, skeletal muscle, kidney, testis, placenta, pancreas, or intestine. Southern blot analysis of restriction fragment length polymorphisms in progeny of interspecific and intersubspecific crosses indicates that mice have a single HCII gene (designated Hcf2), which maps to chromosome 16 between Prm-I and Igl. The murine HCII gene is .sim.7.1 kb in size and consists of at least four exons and three introns. The intron/exon organization is identical to that of the human HCII gene except at the 5' end, where the murine gene may lack a large intron in the 5'-untranslated region. Our results indicate that HCII is more highly conserved than the human and murine homologues of other serpins such as α.sub.1- **antitrypsin** and α.sub.1-antichymotrypsin.

L72 ANSWER 14 OF 21 BIOTECHNO
ACCESSION NUMBER: 1994:24067552 BIOTECHNO
TITLE: Complex formation between protein C inhibitor and prostate-specific antigen in vitro and in human semen
AUTHOR: Christensson A.; Lilja H.
CORPORATE SOURCE: Department of Clinical Chemistry, Lund University, Malmo General Hospital,S-214 01 Malmo, Sweden.
SOURCE: European Journal of Biochemistry, (**1994**), 220/1 (45-53)
CODEN: EJBCAI ISSN: 0014-2956
DOCUMENT TYPE: Journal; Article
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1994:24067552 BIOTECHNO
AB Protein C inhibitor (**PCI**), a **serine-proteinase inhibitor** first purified from human blood plasma, occurs at high concentrations (3-4 μM) in seminal fluid in

both a high-molecular-mass and low-molecular-mass form. Immunochemical data have previously suggested that **PCI** in seminal plasma forms complexes with the most abundant serine proteinase in semen, prostate-specific antigen (PSA). To provide a structural characterization of the **PCI** target, immunodetected as PSA, a procedure was developed to isolate low-molecular-mass and high-molecular-mass-forms of **PCI** from seminal fluid. The high-molecular-mass form of **PCI**, recognized by monoclonal **antibodies** against PSA, was dissociated by alkaline treatment into the low-molecular-mass form of **PCI** and a 33-kDa protein identified as PSA by 25 conclusive steps of N-terminal sequence analysis. We developed a sensitive immunofluorometric assay (IFMA) to measure **PCI**-PSA complexes in body fluids and investigated the rate at which purified PSA may form complexes with purified **PCI**. Formation of complexes detected by this IFMA and the appearance of SDS-stable approximately 90-kDa complexes paralleled loss of PSA activity recorded with chromogenic substrates. The rate of complex formation was slow compared to that reported for **PCI** and activated protein C, but was enhanced up to sixfold in the presence of heparin. Less than 10% of the initial PSA activity remained after 3 h incubation with a sevenfold molar excess of **PCI** and in the presence of heparin. In freshly collected ejaculates, the rate of **PCI**-PSA complex formation measured by IFMA was similar to that observed between the purified proteins, and paralleled the appearance of SDS-stable complexes by immunoblotting. During gel dissolution in freshly collected ejaculates, approximately 40% of immunodetected **PCI** becomes complexed to PSA. Although **PCI** is a slow inhibitor of PSA, complexes between **PCI** and PSA are detected at levels that correspond to an inactivation of up to 5% of the PSA activity in the ejaculate.

L72 ANSWER 15 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1993:23206406 BIOTECHNO
TITLE: Interleukin-6 inhibits corticosteroid-binding globulin synthesis by human hepatoblastoma-derived (Hep G2) cells
AUTHOR: Bartalena L.; Hammond G.L.; Farsetti A.; Flink I.L.; Robbins J.
CORPORATE SOURCE: Istituto di Endocrinologia, University of Pisa, Viale del Tirreno 64,56018 Tirrenia-Pisa, Italy.
SOURCE: Endocrinology, (**1993**), 133/1 (291-296)
CODEN: ENDOAO ISSN: 0013-7227
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1993:23206406 BIOTECHNO
AB Corticosteroid-binding globulin (CBG) belongs to the superfamily of **serine proteinase inhibitors** which include α.sub.1- **antitrypsin**, α.sub.1-antichymotrypsin, and T.sub.4-binding globulin. Interleukin-6 (IL-6), the main mediator of the acute phase phenomenon, increases α.sub.1- **antitrypsin** and α.sub.1-antichymotrypsin synthesis and decreases T.sub.4-binding globulin synthesis by human hepatoblastoma-derived (Hep G2) cells. This effect is predominantly at a transcriptional level. When Hep G2 cells were exposed to different concentrations of IL-6 for variable time intervals, IL-6 caused a dose- and time-dependent decrease in the amount of ¢.sup.3.sup.5S!methionine-labeled CBG immunoprecipitated in the culture medium. This effect could be greatly reduced by preincubation of IL-6 with its neutralizing **antibody** and reversed by removing the cytokine from the culture medium. The secretion rate of CBG was not affected by cell exposure to IL-6. CBG mRNA steady state levels were reduced; changes in mRNA were quantitatively similar to changes in secreted protein. Nuclear run-off assays failed to show a change in the rate of transcription of the CBG gene. These data indicate that IL-6

diminishes CBG synthesis by Hep G2 cells acting at a posttranscriptional level, presumably through a reduced stability of mRNA. In view of the role of IL-6 in the inflammatory process and other acute phase phenomena, these data suggest that its effects on CBG synthesis might influence the bioavailability of cortisol indirectly and play a role in regulating the homeostatic process during these conditions.

L72 ANSWER 16 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1993:23034887 BIOTECHNO
TITLE: Opossum serum α.sub.1-proteinase inhibitor: Purification, linear sequence, and resistance to inactivation by rattlesnake venom metalloproteinases
AUTHOR: Catanese J.J.; Kress L.F.
CORPORATE SOURCE: Molecular/Cellular Biology Dept., Roswell Park Cancer Institute,Buffalo, NY 14263, United States.
SOURCE: Biochemistry, (**1993**), 32/2 (509-515)
CODEN: BICHAW ISSN: 0006-2960
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1993:23034887 BIOTECHNO
AB Opossum (Didelphis virginiana) serum was fractionated with (NH.sub.4).sub.2SO.sub.4 and then chromatographed on DEAE-Sepharose and phenyl-Sepharose. Affinity chromatography on a protein A-Sepharose-**antibody** column removed traces of opossum serum metalloproteinase inhibitors, and resulted in a homogeneous preparation of opossum α.sub.1-proteinase inhibitor (α.sub.1-PI). The inhibitor is a single-chain glycoprotein (17.7% carbohydrate) with an estimated M(r) = 54 000. An opossum liver cDNA library was immunoscreened, and clones containing cDNA encoding for the open reading frame for opossum α.sub.1-PI were isolated. The cDNA inserts contained nucleotide sequences corresponding to the amino- terminal and an internal peptide sequence of opossum α.sub.1-PI which had been separately determined by protein sequence analysis. The entire inserts coded for a protein consisting of a 21-residue signal peptide and a 389-residue mature protein. Opossum α.sub.1-PI shows 51-58% identity with other mammalian α.sub.1-PI amino acid sequences, and the conserved residues expected for a member for the serpin family have been retained. The carbohydrate attachment sites and the reactive site residues (M-S) of opossum α.sub.1-PI are identical to those of human α.sub.1-PI. Opossum α.sub.1-PI formed stable enzyme/inhibitor complexes with trypsin, chymotrypsin, and human neutrophil elastase, but did not react with thrombin or with snake venom serine proteinases. Opossum α.sub.1- PI was inactivated by papain or Pseudomonas aeruginosa elastase, and electrophoretic analysis of the reaction products indicated limited proteolysis in the reactive site loop of the inhibitor. However, opossum α.sub.1-PI retained essentially all its activity when incubated with crude rattlesnake venoms or purified rattlesnake venom metalloproteinases under conditions in which human α.sub.1-PI was readily inactivated. The results are consistent with the hypothesis that opossum α.sub.1-PI is susceptible to cleavage by nonvenom proteinases but is resistant to proteolytic inactivation by venoms of those snakes which it encounters in its environment.

L72 ANSWER 17 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1992:22179320 BIOTECHNO
TITLE: Discovery of a genetic polymorphism of human plasma protein C inhibitor (**PCI**): Genetic survey utilizing isoelectric focusing followed by immunoblotting, immunological and biochemical characterization
AUTHOR: Yasuda T.; Nadano D.; Iida R.; Tanaka Y.; Nakanaga M.; Kishi K.

CORPORATE SOURCE: Department of Legal Medicine, Fukui Medical School, Matsuoka-cho,Fukui 910-11, Japan.
SOURCE: Human Genetics, (**1992**), 89/3 (265-269)
CODEN: HUGEDQ ISSN: 0340-6717
DOCUMENT TYPE: Journal; Article
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1992:22179320 BIOTECHNO
AB The objectives of this study were to determine the genetic basis of the electrophoretic differences of human plasma protein C inhibitors (**PCI**) from 977 individuals. Three discrete **antibodies** were produced against the **PCI** purified from human plasma and peptides that corresponded to the N-terminal 15 amino acid residues and the C-terminal 15 residues of human **PCI**, the chemical structures of which were determined by cDNA sequence analysis. The combined techniques of polyacrylamide gel isoelectric focusing and immunoblotting with these three different **antibodies** resolved the plasma **PCI** into several isoprotein bands, with a pH range of 6-7. These **PCI** isoproteins, however, were not stained by anti-human kallikrein, anti-human protein C or anti-human urokinase **antibodies**. Therefore, each of the **PCI** bands, which were detected by immunoblotting with the anti-**PCI** **antibody** and the two different anti-peptide **antibodies**, were derived from free **PCI**, and not an inactive **PCI** species. Two common phenotypes, designated **PCI** 1 and 1-2, were recognized, and family studies showed that they represented homozygosity or heterozygosity for two autosomal codominant alleles, **PCI**(*)1 and PC1(*)2. A population study of plasma samples collected from 977 Japanese individuals indicated that the frequencies of the **PCI** (*)1 and **PCI**(*)2 alleles were 0.988 and 0.012, respectively.

L72 ANSWER 18 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1990:20373120 BIOTECHNO
TITLE: Elucidating the structural chemistry of glycosaminoglycan recognition by protein C inhibitor
AUTHOR: Kuhn L.A.; Griffin J.H.; Fisher C.L.; Greengard J.S.; Bouma B.N.; Espana F.; Tainer J.A.
CORPORATE SOURCE: Molec./Experimental Med. Dept., Res. Inst. of Scripps Clinic,La Jolla, CA 92037, United States.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (**1990**), 87/21 (8506-8510)
CODEN: PNASA6 ISSN: 0027-8424
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1990:20373120 BIOTECHNO
AB Glycosaminoglycans (GAGs) including heparin accelerate the inhibition of serine proteases by serine protease inhibitors (serpins), an essential process in regulating blood coagulation. To analyze the molecular basis for GAG recognition by the plasma serpin protein C inhibitor (**PCI** ; also known as plasminogen activator inhibitor 3), we have constructed a complete, energy-minimized, three-dimensional model of **PCI** by using the structure of homologous α.sub.1- **antitrypsin** as a template. Sequence analysis, hydrogen-bonding environment, and shape complementarity suggested that the N-terminal residues of **PCI**, which are not homologous to those of α.sub.1- **antitrypsin**, form an amphipathic α-helix, here designated A+ since it precedes the α.sub.1- **antitrypsin** A helix. Electrostatic calculations revealed a single, highly positive surface region arising from both the A+ and H helices, suggesting that this two-helix motif is required for GAG binding by **PCI**. The dominant role of

electrostatic interactions in **PCI**-heparin binding was confirmed by the strong ionic strength dependence of heparin stimulation. The involvement of the A+ helix in heparin binding was verified by demonstrating that an anti-**PCI antibody** that specifically binds the A+ peptide blocks heparin binding.

L72 ANSWER 19 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1986:17183916 BIOTECHNO
TITLE: Complete amino acid sequence of human thyroxine-binding globulin deduced from cloned DNA: Close homology to the serine antiproteases
AUTHOR: Flink I.L.; Bailey T.J.; Gustafson T.A.; et al.
CORPORATE SOURCE: Department of Internal Medicine, University of Arizona College of Medicine, Tucson, AZ 85724, United States.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (**1986**), 83/20 (7708-7712)
CODEN: PNASA6
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
AN 1986:17183916 BIOTECHNO
AB **Antibodies** directed against thyroxine-binding globulin (TBG) have been used to screen a human liver λgt11 expression library. A 1.46-kilobase clone was identified which encodes nearly the complete amino acid sequence, beginning at amino acid 17 of the mature protein. To complete the protein sequence, the cDNA clone was used to identify a genomic clone coding for TBG in a human X chromosome library. The overlapping recombinant clones contained an open reading frame coding for 415 amino acids followed by a polyadenylyation signal (AATAAA) located 275 nucleotides from a TAG termination codon. Beginning at residue 21, the deduced amino acid sequence agrees closely with the known NH.sub.2-terminal sequence of the mature peptide. The preceding 20 amino acid residues and hydrophobic in character and presumably represent a leader sequence. Four glycosylation sites were identified, corresponding to the number determined for the purified protein. DNA blot hybridization revealed a single-copy gene, which by chromosomal analysis was found to be located on the long arm of the X chromosome. Unexpectedly, the nucleotide sequence of TBG is closely homologous to those encoding the plasma serine antiproteases α.sub.1-antichymotrypsin and α.sub.1- **antitrypsin**. However, there is little overall homology between TBG and transthyretin (prealbumin), the other major thyroxine-binding protein of human plasma.

L72 ANSWER 20 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1987:17005226 BIOTECHNO
TITLE: Characterization of a cDNA for human protein C inhibitor. A new member of the plasma serine protease inhibitor superfamily
AUTHOR: Suzuki K.; Deyashiki Y.; Nishioka J.; et al.
CORPORATE SOURCE: Department of Laboratory Medicine, Mie University School of Medicine, Tsu City, Mie 514, Japan.
SOURCE: Journal of Biological Chemistry, (**1987**), 262/2 (611-616)
CODEN: JBCHA3
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
AN 1987:17005226 BIOTECHNO
AB A cDNA library in λ-phage λgt11 containing DNA inserts prepared from human liver mRNA was screened with monoclonal **antibodies** in human protein C inhibitor. Six positive clones were isolated from 6 x 10.sup.6 phages and plaque purified. The cDNA in the phage containing the largest insert, which hybridized to a DNA probe

prepared on the basis of the amino-terminal amino acid sequence of the mature inhibitor, was sequenced. This cDNA insert contained 2106 base pairs coding for a 5'-noncoding region, a 19-amino acid signal peptide, a 387-amino acid mature protein, a stop codon, and a long 3'-noncoding region of 839 base pairs. Based on the amino acid sequence of the carboxyl-terminal peptide released by cleavage of protein C inhibitor by activated protein C as well as by thrombin, the reactive site peptide bond of protein C inhibitor is Arg.sup.3.sup.5.sup.4-Ser.sup.3.sup.5.sup.5. Five potential carbohydrate-binding sites were found in the mature protein. The high homology of the amino acid sequence of protein C inhibitor to the other known inhibitors clearly demonstrates that protein C inhibitor is a member of the superfamily of serine protease inhibitors including α.sub.1-antichymotrypsin, α.sub.1- **antitrypsin**, antithrombin III, ovalbumin, and angiotensinogen. Based on the difference matrices for these proteins, we present possible phylogenetic trees for these proteins.

L72 ANSWER 21 OF 21 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1986:16002316 BIOTECHNO
TITLE: Cloning and sequence of a cDNA coding for the human β-migrating endothelial-cell-type plasminogen activator inhibitor
AUTHOR: Ny T.; Sawdey M.; Lawrence D.; et al.
CORPORATE SOURCE: Department of Immunology, Scripps Clinic and Research Foundation, La Jolla, CA 92037, United States.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (**1986**), 83/18 (6776-6780)
CODEN: PNASA6
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
AN 1986:16002316 BIOTECHNO
AB A λgt11 expression library containing cDNA inserts prepared from human placental mRNA was screened immunologically using an **antibody** probe developed against the β-migrating plasminogen activator inhibitor (β-PAI) purified from cultured bovine aortic endothelial cells. Thirty-four positive clones were isolated after screening 7 x 10.sup.5 phages. Three clones (λ1.2, λ3, and λ9.2) were randomly picked and further characterized. These contained inserts 1.9, 3.0, and 1.9 kilobases (kb) long, respectively. Escherichia coli lysogenic for λ9.2, but not for λgt11, produced a fusion protein of 180 kDa that was recognized by affinity-purified **antibodies** against the bovine aortic endothelial cell β-PAI and had β-PAI activity when analyzed by reverse fibrin autography. The largest cDNA insert was sequenced and shown to be 2944 base pairs (bp) long. It has a large 3' untranslated region ¢1788 bp, excluding the poly(A) tail! and contains the entire coding region of the mature protein but lacks the initiation codon and part of the signal peptide coding region at the 5' terminus. The two clones carrying the 1.9-kb cDNA inserts were partially sequenced and shown to be identical to the 3.0-kb cDNA except that they were truncated, lacking much of the 3' untranslated region. Blot hybridization analysis of electrophoretically fractionated RNA from the human fibrosarcoma cell line HT-1080 was performed using the 3.0-kb cDNA as hybridization probe. Two distinct transcripts, 2.2 and 3.0 kb, were detected, suggesting that the 1.9-kb cDNA may have been copied from the shorter RNA transcript. The amino acid sequence deduced from the cDNA was aligned with the NH.sub.2-terminal sequence of the human β-PAI. Based on this alignment, the mature human β-PAI is 379 amino acids long and contains an NH.sub.2-terminal valine. The deduced amino acid sequence has extensive (30%) homology with α.sub.1- **antitrypsin** and antithrombin III, indicating that the β-PAI is a member of the **serine proteinase inhibitor** (serpin)

superfamily.